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PCT/KR2004/003546

REC'D 09 DEC 2005

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference MDB 19PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. **PCT/KR2004/003546**	International filing date *(day/month/year)* **30 DECEMBER 2004 (30.12.2004)**	Priority date *(day/month/year)* 30 DECEMBER 2003 (30.12.2003)

International Patent Classification (IPC) or national classification and IPC

IPC7 A61K 31/343, A61K 35/78, A61P 3/04

Applicant

MD BioAlpha Co., Ltd. et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☒ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
21 JULY 2005 (21.07.2005)	22 NOVEMBER 2005 (22.11.2005)
Name and mailing address of the IPEA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer LEE, Mi Jeong Telephone No. 82-42-481-5601

Form PCT/IPEA/409 (cover sheet) (April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. I Basis of the report

1. With regard to the **language,** this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☒ This report is based on translations from the original language into the following language English, which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☒ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this reort as "originally filed" and are not annexed to this report):*

   ☒ the international application as originally filed/furnished

   ☐ the description:
   pages _____ as originally filed/furnished
   pages* _____ received by this Authority on _____
   pages* _____ received by this Authority on _____

   ☐ the claims:
   pages _____ as originally filed/furnished
   pages* _____ as amended (together with any statment) under Article 19
   pages* _____ received by this Authority on _____
   pages* _____ received by this Authority on _____

   ☐ the drawings:
   pages _____ as originally filed/furnished
   pages* _____ received by this Authority on _____
   pages* _____ received by this Authority on _____

   ☐ the sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:
   ☐ the description, pages _____
   ☐ the claims, Nos. _____
   ☐ the drawings, sheets _____
   ☐ the sequence listing *(specify)* : _____
   ☐ any table(s) related to sequence listing *(specify)* : _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   ☐ the description, pages _____
   ☐ the claims, Nos. _____
   ☐ the drawings, sheets _____
   ☐ the sequence listing *(specify)*: _____
   ☐ any table(s) related to sequence listing *(specify)* : _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has, within the applicable time limti:
   - ☐ restricted the claims
   - ☐ paid additional fees
   - ☐ paid additional fees under protest and, where applicable, the protest fee
   - ☐ paid additional fees under protest but the applicable protest fee was not paid
   - ☐ neither restricted nor paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is :
   - ☐ complied with.
   - ☐ not complied with for the following reasons:

Group I. Claims 1– 39 : Composition of tanshinone derivatives for treatment of obesity and metabolic syndrome

Group II. Claims 40, 41 : Preparation methods of Tanshen extract.

Although both Group I and Group II relate to Tanshen, they do not have common technical characteristics.

4. Consequently, this report has been established in respect of the following parts of the international application :
   - ☒ all parts.
   - ☐ the parts relating to claims Nos.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 - 41	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1 - 41	NO
Industrial applicability (IA)	Claims	1 - 41	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents are referred to in this report:

D1: Arch. Pharm. Res. Vol.25(4), pp.446-448 (2002)
D2: Planta Med. Vol.68(12), pp.1077-1081 (2002)
D3: Chem. Pharm. Bull. Vol.45(8), pp.1306-1311 (1997)
D4: Planta Med. Vol.55(1), pp.51-54 (1989)
D5: KR 2001-0019147 A (15. Mar. 2001)

1. Novelty

Claims 1-27, 35-39 of the present invention relate to a composition of Tanshen (Salvia miltiorrhiza, Perovska abrotanoides) extract comprising a variety of tanshinone derivatives such as tanshinone I, cryptotanshinone, and tanshinone VI for treatment of obesity and metabolic syndromes. Claim 28 relates to the said composition for treatment of obesity, diabetes melitus, arteriosclerosis, hypertension, hyperlipoidemia, liver diseases, ischemic diseases.

Claim 29 relates to a composition of Tanshen extract comprising a variety of tanshinone derivatives for increasing the activity of 5'-AMP-activated protein kinase. Claims 30-34 relate to a composition of Tanshen extract comprising a variety of tanshinone derivatives for treatment of diabetes, obesity, hyperlipoidemia, liver cell damage, ateriosclerosis, hypertension, and ischemic diseases by increasing the activity of 5'-AMP-activated protein kinase.

Claims 40, 41 of the present invention relate to a method for preparing the extract of Tanshen comprising a) extracting Tanshen using water or organic solvent, b) concentrating the extract after filtering the crude extract obtained from a), and c) optionally, eliminating the residual solvent in the concentrated extract.

D1 discloses that tanshinone derivatives obtained from Salvia miltiorrhiza inhibit the activity of diacylglycerol acyltransferase.
D2 discloses the hepatoprotective effect of dihydroisotanshinone I against menadione-induced cytotoxicity in a primary culture of rat hepatocytes.
D3 discloses that tanshinone derivatives isolated from the root of Salvia miltiorhiza Bunge show strong aldose reductase inhibitory activity. (Continued on the Supplemental Sheet.)

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:

Box V.

D4 discloses that tanshinone derivatives such as tanshinone I, cryptotanshinone, and tanshinone VI can protect the myocardium against ischemia-induced derangements.
D5 discloses that the anti-hypertensive and anticholesterol effect of tanshen extract are not significant. D5 also discloses a method for preparing the extract of Tanshen comprising extracting Tanshen using water or organic solvent and freeze-drying the extract obtained.

The active ingredient in claims 1-28, 35-39 of the present invention is an extract of Tanshen, while the active ingredients in D1-D4 are specific tanshinone derivatives. D5 gives a negative indication in developing Tanshen extract as anti-hypertensive and anticholesterol drug.

None of D1-D5 discloses that Tanshen extract can exert the said pharmacological effects by increasing the activity of 5'-AMP-activated protein kinase, which is described in claims 29-34 of the present invention.

The preparation method in D5 differs from the disclosure in claims 40, 41 in that freeze-drying method is used to concentrate the crude extract of Tanshen.

Therefore, claims 1-41 of the present invention are considered to be novel over D1-D5 [Article 33(2) PCT].

2. Inventive Step

The medical uses of Tanshen extract comprising tanshinone derivatives in claims 1-28, 35-39 can be easily expected from D1-D4 by a man skilled in the art.
Claims 29-34 describe a new pharmacological mechanism, but it does not make any difference in the medical use invention to find a new mechanism, as long as the eventual medical uses are same.
Thus, the inventive step of claims 1-39 cannot be acknowledged over D1-D4.

The preparation methods of Tanshen extract in claims 40, 41 are very common procedures in the art and freeze-drying procedures in D5 can be easily exchanged into vacuum-drying or any other concentrating procedures by a man skilled in the art.
Therefore, the inventive step of claims 40, 41 cannot be acknowledged over D5 [Article 33(3) PCT].

3. Industrial Applicability

The subject-matter of claims 1-41 appears to be industrially applicable [Article 33(4) PCT].